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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,309	08/20/2001	Gregory M. Fahy	FAH02 P-300A	7331

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	7

DATE MAILED: 04/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,309	FAHY, GREGORY M.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Status of Application, Amendments and/or Claims

The amendment filed 20 August 2001 (Paper No. 2) has been entered in full. Claims 1-15 and 23-31 were cancelled. New claims 32 and 33 were added.

The information disclosure statement filed 03 December 2001 (Paper No. 3) was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

The amendment filed 26 March 2002 (Paper No. 4) has been entered in full. New claim 34 was added.

Applicant's species election of DHEA, human growth hormone and chromium picolinate in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Election was made **without** traverse in Paper No. 6 (30 December 2002).

Claim Objections

Claims 20, 21, are objected to because of the following informalities: The instant claims encompass non-elected inventions (species) and require amendment to limit to elected invention. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 16, 17, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is drawn to a method for transplanting organs and grafting tissue into a patient comprising: restoring immune system function by regenerating the patient's involuted thymus; injecting the immunological equivalent of the tissue or organ to be transplanted into the patient, into the regenerated thymus (or, in the case of bone marrow cell, peripherally); and then transplanting said organ or grafting said tissue.

The claim is indefinite because it is drawn to regenerating the patient's involuted thymus but the steps comprise injecting the immunological equivalent into the regenerated thymus (which means the thymus is already regenerated). Thus, the steps of regenerating the involuted thymus have not been taught. The claim does not set forth any steps involved in the method/process (regenerating an involuted thymus). It is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 16 is indefinite because the term "immunological equivalent" is a relative term which renders the claim indefinite. The term "immunological equivalent" is not defined by the claim, the specification does not provide a standard for ascertaining the

requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 17, 18 recite the limitation "intrathymic injection". There is insufficient antecedent basis for this limitation in the claim.

Regarding claim 19, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 20, 21 and 22 recite the limitation "step of regenerating". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-22, 32-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claim is drawn to a method for transplanting organs and grafting tissue into a patient comprising: restoring immune system function by regenerating the patient's involuted thymus; injecting the immunological equivalent of the tissue or organ

to be transplanted into the patient, into the regenerated thymus (or, in the case of bone marrow cell, peripherally); and then transplanting said organ or grafting said tissue.

Greenstein *et al.* (J. Endocr. 1987, IDS submitted by Applicant) teach orchidectomy is associated with an increased immune response to antigen challenge. Greenstein demonstrates that the thymus, which had virtually disappeared in old rats, was greatly restored after orchidectomy. Greenstein also demonstrates that regeneration of an age-involuted thymus can be accomplished in rats using an analogue of luteinizing hormone-releasing hormone (LHRH). The LHRH analogue, however, also reduced testosterone concentrations to levels measured in orchidectomized rats. McCormick *et al.* (Aging:Immunology and Infectious Disease, 1991, IDS submitted by Applicant) teach that regeneration of an age-involuted thymus can be accomplished in rats using growth hormone (GH). However, there was no significant improvement of cellular immune function and most importantly, there was a high incidence of hepatic tumors noted in the growth hormone treated mice. Goff *et al.* (Clin. Exp. Immunol., 1987, IDS submitted by Applicant, Paper No. 3) discloses the dubious nature of discerning a regenerated thymus. Goff states, "a change (or lack of change) in thymic morphology does not prove increased or decreased thymic function: immunological or endocrine function must also be assessed" (page 585, 3rd paragraph).

Perico *et al.* (J. American Soc. Neph., 1991, IDS submitted by Applicant) does not conclusively demonstrate that immunosuppressive drugs do not interfere with the functional properties of the thymus. It has been shown that cyclosporin (CsA) and steroids used to inhibit T cell activation and to deplete them from peripheral circulation

also induce changes in the structure and function of the thymus, which include a decrease in thymus epithelial and cortical cells. Perico states, "all of these experiments do not yet allow conclusions to be made on whether the theoretical possibility of achieving donor-specific tolerance to allografts would possibly apply to human transplantations". "One can not exclude the possibility that the mechanism we and others have described only applies to the peculiar immune system of rats" (page 1069, last paragraph). Odorico *et al.* (Transplantation, 1993) teach that the efficacy of tolerance induction by the intrathymic injection of donor spleens cells appears to depend on the concurrent administration of antilymphocyte serum (ALS) in rats. Omission of ALS from the preparative regimen or substitution of CsA (a non-T-cell depleting immunosuppressant) for ALS, abrogated the ability of an intrathymic splenocyte injection to promote unresponsiveness to cardiac allografts, suggesting that a transient depletion of mature peripheral T cells is required for tolerance induction by this method.

The instant specification fails to demonstrate that a patient can have an involuted thymus regenerated, then undergo an intrathymic injection and organ transplant or tissue graft. Furthermore, Applicants have not demonstrated that this combined method would be successful or better than the methods known in the art for organ transplant/tissue grafts. The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure. The instant specification only teaches the administration of arginine and DHEA and HGH and DHEA. The specification does not provide guidelines to determine thymic atrophy or involution. The specification fails

to teach that a thymus can be regenerated upon administration of human growth hormone and DHEA or human growth hormone and chromium picolinate in a patient. The disclosure does not provide immunological or endocrine assays or employ experiments such as magnetic resonance imaging or morphology studies which would discern that a thymus has been regenerated. The specification provides no guidance or working examples for intrathymic injection. The specification fails to teach or disclose working examples for transplanting an organ or grafting of tissue. The specification does not consider factors such as rejection, age-related thymic involution versus other types of thymic involution, the side effects of immunosuppressants, ALS versus CsA, the high incidence of tumors and other side effects associated with GH. For the reasons discussed above, such experimentation would be undue for one skilled in this art at the time the invention was made.

Due to the large quantity of experimentation necessary to regenerate an involuted thymus, administer an intrathymic injection and transplant an organ or tissue, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the state of the prior art which establishes the unpredictability of intrathymic injections and organ/graft transplants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
March 28, 2003

Elyabeth C. Kemmerer

Director, TC 1600